REMARKS/ARGUMENTS

In this Amendment, the status of the claims is as follows: claims 1-49, 53, 76, 96, 105 and 106 have been canceled; claims 50, 52, 54, 73, 75, 77, 97-100 and 104 are currently amended; claims 51, 55-72, 74, 78-93, 101-103 and 107-124 were previously presented; claims 94 and 95 are original claims; and claims 125-131 have been newly added. It is submitted that no new matter has been added by virtue of the amended and new claims, which are supported by the disclosure and claims of the application as originally filed and by the previously presented claims.

Specifically, claims 52, 75, 99 and 100 have been amended for clarity or to correct clerical oversights. In amended claims 50, 73, 97 and 98, support for the recitation that one or more rapidly dispersible matrix-forming bulking/releasing agents, or the combination of matrix-forming bulking agents and matrix-forming releasing agents, are present in an amount of between 0.1% w/w and 90% w/w, said amount permitting the dried solid dosage form, upon reconstitution in an aqueous environment, to revert to a suspension having no more than about 20% by weight of particle aggregation or agglomeration compared with the amount of aggregation or agglomeration of particles comprising a pre-dried suspension, is found in the as-filed specification on page 7, lines 12-14 and on page 8, lines 25-26. This disclosure corresponds to the same disclosure of published application number 20020106403 A1, page 6, last three lines of [0018] and on page 67, second through fourth lines of [0023]. Support for the amount of bulking/releasing agent in amended claims 54 and 77 is found in the as-filed specification on page 7, line 3 (and on page 6, last two lines of [0018]). Support for new claims 125-128 is found in the as-filed specification on page 8, lines 25-28 (and on page 7, lines 2 through 5 of [0023]).

Accordingly, claims 50-52, 54-75, 77-95, 97-104 and 107-131 are currently pending in this application.

Change of Correspondence/Mailing Address and Customer Number

Applicants request that the correspondence/mailing address and customer number for this application be recognized as "MINTZ, LEVIN, COHN, FERRIS, GLOVSKY and POPEO,

P.C., The Chrysler Center, 666 Third Avenue, New York, New York 10017, **Customer No. 35437** and officially changed in the U.S. Patent and Trademark Office.

On October 8, 2004, Applicants submitted Form PTO/SB/122 "Change of Correspondence Address" in this application. A review of the Image File Wrapper for this application on the U.S. PTO PAIR website shows that the above Change of Correspondence Address paper and was received was date-stamped "OCT 08 2004" by the U.S. PTO.

On December 16, 2004, Applicants submitted a formal Revocation of Power of Attorney by Assignee, New Power of Attorney and Change of Correspondence Address document, along with accompanying documentation, in this application. A review of the Image File Wrapper for this application on the U.S. PTO PAIR website shows that the Revocation of Power of Attorney by Assignee, New Power of Attorney and Change of Correspondence Address document was received and date-stamped "DEC 16 2004" by the U.S. PTO.

Although the Image File Wrapper for this application on the U.S. PTO PAIR website shows that the above papers were received by the U.S. PTO as-filed, there is a paper described as "Change of Address" and dated December 23, 2004, which is listed in the U.S. PTO PAIR Image File Wrapper. It appears from this paper that the U.S. PTO erroneously set both the correspondence address and the maintenance fee address to the **prior** customer number in this application rather than changing the correspondence address to the current address and customer number as Applicants have formally requested.

Accordingly, in view of the above, appropriate correction of the Patent Office records to reflect the current correspondence address (i.e., MINTZ, LEVIN, COHN, FERRIS, GLOVSKY and POPEO, P.C., The Chrysler Center, 666 Third Avenue, New York, New York 10017) and customer number (i.e., Customer Number 35437) for this application is now requested.

The claims fulfill the requirements of 35 U.S.C. § 103(a)

WO 98/07414

Claims 50-124 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over previously-cited international publication, WO 98/07414.

The Examiner alleges that WO 98/07414 "discloses the same process of preparation for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are coated with at least two surfactants; one of the surfactants is a phospholipid (surface acting agent)". The Examiner further contends that "[t]he process by WO differs from the claimed process ... in that, the bulking agent is added along with the active agent and the surface modifiers" and cites to the paragraph bridging pages 7 and 8 of WO 98/07414 as teaching "mannitol and other agents may be added to adjust the final formulation to isotonicity as well as a stabilizing agent during drying". According to the Examiner, from this teaching it would have been obvious to one of ordinary skill in the art that the addition of mannitol is a manipulatable parameter, which can be added either before or after the homogenization step with the expectation of obtaining the best possible stabilized product.

Applicants note that the rejection of claim 96 is mooted in view of its prior cancellation.

It is respectfully submitted that Applicants' presently claimed process is neither the same as nor obvious in view of the disclosure of WO 98/07414. It is well understood that the presently claimed invention must be considered as a whole in determining differences between the prior art and the presently claimed invention. M.P.E.P. §2141.02. In addition, all claim limitations must be taught or suggested by the cited art reference. M.P.E.P. §2143.03. In the instant case, the presently claimed process, considered in its entirety, involves inventive steps and elements associated therewith that are different and distinct from the method disclosed and taught in WO 98/07414.

Specifically, the method disclosed in WO 98/07414 (see, e.g., page 9 of WO 98/07414) is directed to making submicron sized particles that do not aggregate upon storage. WO 98/07414 neither addresses nor suggests a process of making rapidly dispersible solid dosage

forms of a drug. The method contemplated and described in WO 98/07414 involves the following:

- particles of a compound of interest are mixed with phospholipid and surfactant to form a premix; and

- the size of the particles is reduced by applying a form of energy to the mixture to achieve the characteristic that the volume-weighted mean particle size values of the resulting compound are at least 50% smaller than the size values of particles produced in the absence of surfactant.

WO 98/07414 discloses that mannitol "... may be added to adjust the final formulation to isotonicity as well as [to act as] a stabilizing aid during drying." (page 8, lines 4-6 of WO 98/07414). In the Examples of WO 98/07414, mannitol, drug, phospholipid and surfactant form the premix, which is then subjected to a high energy procedure to reduce the size of the particles, which are stored. WO 98/07414 does not teach or suggest a process of producing a solid dosage form of a drug having particular dispersibility characteristics.

In distinction to the disclosure of WO 98/07414, Applicants' presently claimed process requires that a suspension including drug, one or more surface stabilizing agents, at least one of which is a phospholipid, or combinations thereof, is admixed with one or more bulking/releasing agents, or with a combination of a bulking agent and a releasing agent. The process includes particle fragmentation and drying the admixture. In accordance with Applicants' presently claimed process, the one or more rapidly dispersible matrix-forming bulking/releasing agents, or the combination of matrix-forming bulking agent and matrix-forming releasing agent, are present the process in an amount of between 0.1% w/w and 90% w/w of the aqueous suspension, said amount permitting the resulting dried solid suspension, upon reconstitution in an aqueous environment, to revert to a suspension having no more than about 20% by weight of particle aggregation or agglomeration compared with the amount of aggregation or agglomeration of particles comprising a pre-dried suspension.

WO 98/07414 is silent regarding a process in which bulking/releasing agents (of which mannitol is but one example) are present in amounts described in Applicants' presently claimed

invention so as to permit the resulting dried solid suspension, upon reconstitution in an aqueous environment, to revert to a suspension having no more than about 20% by weight of particle aggregation or agglomeration compared with the amount of aggregation or agglomeration of particles comprising a pre-dried suspension. Moreover, WO 98/07414 does not suggest or contemplate that a solid dosage form of the drug particles possesses the dispersity characteristics resulting from the presence of one or more matrix-forming/bulking agents in the amounts described and having the functions as set forth in the presently claimed process.

WO 98/07414 does not recognize and fails to teach a process of achieving a rapidly dispersible solid form of a drug. Without the knowledge that is provided by Applicants' disclosure and the presently claimed inventive process, one having skill in the art is not led to Applicants' claimed invention based on the method disclosed and exemplified in WO 98/07414. The general statement in WO 98/07414 that mannitol "... may be added to adjust the final formulation to isotonicity as well as [to act as] a stabilizing aid during drying" provides no motivation for the skilled practitioner to modify the method of WO 98/07414 to arrive at Applicants' process in which matrix-forming agent, bulking agent, or combinations thereof, contribute to the process so as to provide rapidly dispersible solid dosage forms of a drug in which the solid dried drug particles have essentially the same degree of dispersibility after contact with an aqueous environment as do the particles prior to the drying process. The new and surprising results of Applicants' presently claimed process are clearly demonstrated in the formulations presented in the as-filed specification on page 10, Table 1, Examples/Formulation Numbers 6-10.

In sum, the steps, elements and amounts thereof in Applicants' presently claimed process, considered as a whole, are not made obvious by the disclosure of WO 98/07414, which generally mentions the addition of mannitol as an isotonicity adjuster or as a stabilizing aid. No requirements for amounts of mannitol, or for the use of mannitol with other elements and/or bulking/releasing agents, to provide a highly dispersible, solid dosage form of a drug are found in WO 98/07414. Thus, based on the disclosure of WO 98/07414 for all that it teaches, one skilled in the art is not led to make the modifications that would be necessary to arrive at

Applicants' presently claimed process considered as a whole with a reasonable expectation of success in obtaining what is presently claimed.

WO 98/07414 does not teach or suggest all of Applicants' claim limitations, as is required pursuant to M.P.E.P. §2143. Consequently, WO 98/07414 fails to make obvious Applicants' invention as presently claimed. In view of the foregoing, it is submitted that a *prima facie* case of obviousness of the presently claimed invention has not been shown. Withdrawal of this rejection is thus respectfully requested.

Yarwood in combination with Green, Na and WO 98/07414

Claims 50-124 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Yarwood (U.S. Patent No. 5,827,541), (hereinafter "Yarwood"), in combination with Green (U.S. Patent No. 5,976,577, of record), (hereinafter "Green"), or Na (U.S. Patent No. 5,326,552), (hereinafter "Na"), or WO 98/07414, cited by themselves or in combination.

According to the Examiner, Yarwood discloses "a process for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are coated with a surfactant (surface modifying agent)", namely poloxamer.

It is submitted that Yarwood, in combination with the other cited references as discussed above and below, do not make obvious Applicants' presently claimed invention. Yarwood and the combined cited art do not teach or suggest all of Applicants' claim limitations, as is required pursuant to M.P.E.P. §2143.03. In the instant case, Applicants' presently claimed process and the process described by Yarwood in combination with Green, Na and WO 98/07414 reflect distinct and different processes of preparing rapidly disintegrating dosage forms of a hydrophobic active substance.

As stated in M.P.E.P. §2143.01, citing to *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990),

> the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art

> also suggests the desirability of the combination. (Emphasis in original).

It is submitted that Yarwood, taken in combination with the cited art references of Green, Na and WO 98/07414, does not provide the suggestion to add a phospholipid to Yarwood's disclosed process. Yarwood simply does not teach or exemplify a process that involves the use of more than one surfactant at least one of which must be a phospholipid, as is required in Applicant's presently claimed process. Without any teaching or guidance provided by Yarwood and the cited art, it would not have been obvious to use more than one surfactant, or surfactant and phospholipid together, in Yarwood's process, as one would not have a reasonable expectation, based on Yarwood's disclosure and the teaching of the art, that more than one surfactant, or a combination of surfactant and phospholipid, would result in a suspension having the property of rapid disintegration as specified by Yarwood.

The Examiner opines that the cited art teaches various ingredients, e.g., surfactants and phospholipids, which are used to coat active agents. However, Applicants' claimed invention is not directed to a composition containing recited ingredients, but is instead directed to a process having steps, related elements and amounts thereof, which perform and function as described and which are distinct and different from the processs and included elements that are disclosed in the cited art.

Applicants respectfully submit that the processes of the cited art involve steps and related elements therein that are plainly distinguished from those of the presently claimed invention in numerous ways. It is respectfully submitted that the invention being claimed should not be lost sight of in considering the disclosures and teachings of the art.

Illustratively, as specifically taught and exemplified by Yarwood (See, e.g., the Abstract; Col. 1, lines 60-65; and the Example, Col. 5, lines 1-18), Yarwood's process of preparing an oral rapidly disintegrating dosage form involves the following steps and elements:

- forming a suspension containing an active substance and a pharmaceutically acceptable surfactant, together with a carrier material (e.g., gelatin or other materials as set forth at Col. 4, lines 4-14);

- forming discrete units of the suspension; and
- removing solvent from the discrete units.

The discrete units of the suspension are in the form of liquid units (e.g., within the pockets of a mold); solid units (e.g., frozen units); or gelled units. (Col. 3, lines 8-11 and Col. 4, lines 15-28).

The Examiner has cited both Green and Na for their suggestion to use phospholipid as a coating material and as providing knowledge that phospholipids are surface modifiers (03/30/05 Office Action, pages 6 and 7). However, the suggestion of phospholipid use, in combination with the complete teachings of Yarwood, do not make obvious Applicants' presently claimed invention. The combination of Yarwood, Green, Na and WO 98/07414 does not teach or suggest all of the claim limitations as is required for a finding of obviousness in accordance with M.P.E.P. §§2142 and 2143.

Combining Yarwood's process with the teaching of Green and Na might result in Yarwood's using a phospholipid as the surfactant in Yarwood's process. However, this does not make obvious Applicants' presently claimed process, since Yarwood's process does not include, and is not contemplated to include, more than one surfactant or a combination of surfactant and phospholipid, in contrast to Applicants' claimed process. Further, a combination of the teachings of Yarwood, Green, Na and WO 98/07414 does not result in a suggestion or teaching that would lead one to devise a process including matrix forming bulking/releasing agents present in the amounts specified in Applicants' process so as to achieve the characteristics of drug particle dispersibility as discovered by Applicants.

The reasons that the combined references fail to make obvious the presently claimed invention are as follows. First, in contrast to Applicants' claimed invention, Yarwood does not teach adding more than one surfactant, or that a phospholipid must be present instead of, or in addition to, the one surfactant that is required in Yarwood's process. As the Examiner has recognized (03/30/05 Office Action, page 4), mixtures or combinations of surfactants are neither disclosed nor exemplified by Yarwood. Further, surfactant is not taught or exemplified to be used in combination with a phospholipid, nor is a phospholipid disclosed as a surfactant. In

spite of this, the Examiner concludes, without providing supporting evidence, that "it would have been obvious to one of ordinary skill in the art to use phospholipids, which are well know [*sic*] surfactants, in the process of Yarwood, based on the suggestion in Yarwood that "any surfactant which fulfills the requirement of pharmaceutical acceptability may be used" and the knowledge that a phospholipid can be a surfactant.

Applicants respectfully submit that even if, *in arguendo*, a phospholipid were to be used as the pharmaceutically acceptable surfactant in Yarwood's process, Yarwood teaches that the phospholipid would be used alone in the process with a carrier material. Therefore, in consideration of Yarwood's teaching, one skilled in the art would simply replace the surfactant with phospholipid to carry out Yarwood's process. There is no teaching or disclosure in Yarwood to combine a phospholipid with another surfactant, or to use a phospholipid as a surfactant with another type of surfactant in Yarwood's process. This stands in plain contrast to Applicants' presently claimed process.

Further, based on a consideration of Yarwood's teaching and disclosure as a whole, there is no reasonable expectation that one skilled in the art would successfully achieve the disintegration properties of Yarwood's dosage form if more than one surfactant were used in Yarwood's contemplated process, or if a surfactant in combination with a phospholipid were to be used in the process. Thus, there is no motivation or suggestion provided by Yarwood in combination with Green, Na and WO 98/07414 to add more than one surfactant/phospholipid, or to add a surfactant and phospholipid in combination with bulking/releasing agents, or combinations thereof, in amounts as presently claimed by Applicants, so as to arrive at a solid dosage form having the properties and characteristics of the presently claimed invention.

Second, Yarwood is silent regarding a process in which a suspension is subjected to a particle fragmentation process after the suspension is formed. Instead, Yarwood's suspension is formed into discrete units of liquid, solid, or gelled material, which are subjected to a drying process to produce the final dosage form (Col. 5, lines 15-18).

Third, in Yarwood, unlike Applicants' presently claimed invention, the disclosed suspension is formed into discrete units that are frozen or gelled before drying. (Col. 3, lines 8-

60). There is no suggestion or motivation provided by Yarwood combined with the cited art to perform a particle fragmentation process in Yarwood's process prior to forming discrete units and removing solvent therefrom. Yarwood combined with Green, Na and WO 98/07414 do not make obvious Applicants' claimed process considered in its entirety, as there is no suggestion provided by this combination to modify the teachings of the references so as to arrive at the presently claimed invention considered as a whole.

Although the cited references may disclose discrete ingredients, inventiveness in the instant case resides in Applicants' presently claimed process, with its recited steps and the elements therein considered as a whole. The teaching and disclosure of Green, Na and WO 98/07414 do not compensate for the deficiencies in Yarwood's teaching and process and, combined with Yarwood, do not make obvious Applicants' presently claimed process.

As can be seen from the Examples/Formulations in Table 1 on page 10 of the instant specification as-filed, Applicants' claimed process comprising admixing drug, surfactant, phospholipid and bulking/releasing agent provides dried solid particles having essentially the same dispersibility both pre- and post-lyophilization, i.e., drying. (See, Table 1, Formulations 6-10, last two columns, and the description thereof on page 11, lines 23-25 of the as-filed specification). These elements of the presently claimed invention are neither taught nor suggested by Yarwood and the cited art, either alone or in combination.

Applicants point out that Yarwood's sole Example (Col. 5, lines 1-24) does not include a phospholipid in combination with an active agent, one or more surface stabilizing agents and one or more bulking/releasing agents. Even if a phospholipid were to be used in Yarwood's process as a surfactant, Yarwood's Example is akin to Example/Formulation 4 presented in Table 1 on page 10 of Applicants' as-filed specification. Example/Formulation 4 in Table 1 demonstrates that, without the appropriate combination of elements in the process taught by Applicants, i.e., with phospholipid alone, the resulting particles possess inferior attributes of disintegration time and particle size when assessed both in pre-dried and post-dried form, i.e., following reconstitution. Yarwood's process in combination with the cited art is not only distinct from, but is plainly inferior to, Applicants' presently claimed process. It is therefore submitted that, without knowledge of Applicants' inventive process and contrary to the

Examiner's statement, it would not be "obvious to one of ordinary skill in the art to manipulate the basic process of Yarwood with the expectation of obtaining the best possible results". (03/30/05 Office Action, page 5).

The Examiner further remarks that based on the teaching of WO 98/07414, "it would be obvious ... that the addition of mannitol is a manipulatable parameter" and that mannitol "can be added either before or after the homogenization step with the expectation of obtaining the best possible stabilized product." (03/30/05 Office Action, page 5). Applicants contend that while WO 98/07414 may teach a method for stabilizing microparticles upon storage, this reference does not teach or suggest a process, such as that presently claimed by Applicants, of producing a rapidly dispersible solid dosage form of a drug. WO 98/07414, considered for all that it teaches, does not lead the ordinarily skilled artisan to arrive at Applicants' presently claimed process having the distinctive combinations of steps, elements and amounts thereof, to produce a solid dosage form of a drug and resulting in the dispersibility properties as discovered by Applicants.

In short, it is submitted that Yarwood, Green, Na and WO 98/07414, taken alone or in combination, do not teach or suggest all of Applicants' claim limitations and do not make obvious Applicants' presently claimed process. None of these references, alone or in combination, teach or contemplate a process such as that presently claimed by Applicants in which a homogenous suspension of drug and surface stabilizing agent and/or phospholipid is admixed with one or more rapidly dispersible matrix-forming bulking/releasing agents, or a combination of a matrix-forming bulking agent and a matrix-forming releasing agent, present in an amount of between 0.1% w/w and 90% w/w, such that a dried solid suspension, upon reconstitution in an aqueous environment, is able to revert to a suspension having no more than about 20% by weight of particle aggregation or agglomeration compared with the amount of aggregation or agglomeration of particles comprising a pre-dried suspension.

In view of the foregoing, it is submitted that the differences between Yarwood's process, combined with the cited art, and Applicants' presently claimed process are clear. Applicants' presently claimed process is unobvious over Yarwood's teaching in combination with the teachings of Green, Na and WO 98/07414, taken alone or in combination. Accordingly, withdrawal of this rejection under 35 U.S.C. §103(a) is respectfully requested.

Double Patenting

U.S. Patent No. 5,922,355

Claims 50-124 were rejected under the judicidally created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-11 of U.S. Patent No. 5,922,355 ("the '355 patent"). The Examiner states that the conflicting claims are not identical, but are allegedly not patentably distinct from each other because the claims in the '355 patent, which are drawn to "a process of preparing microparticles of water insoluble drugs mixing the drug, a phospholipid and another surfactant and applying energy to reduce particle sizes", recite comprising language and that "applicant's intent to include bulking material such as mannitol in the comprising language is clear from the examples" in the cited patent. The Examiner opines that the "instant steps of adding the bulking materials" are deemed to be included in the patented method claims.

Applicants disagree with this rejection and submit that although the claims of the '355 patent contain comprising language, there is no teaching or disclosure in the '355 patent that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success.

The mere disclosure of mannitol in the Examples of the specification of the '355 patent does not make obvious Applicants' inventive process, considered in its entirety, including the steps and elements therein, which specify and describe particular amounts and functions of bulking/releasing agents. The combination of steps and elements therein, including bulking/releasing agents, contributes to the newly described properties of high dispersibility imparted to a solid dosage form that is produced by Applicants' presently claimed process. The steps and elements therein that constitute the process of the presently claimed invention are not at all found in the disclosure of the '355 patent.

The disclosure relating to mannitol in the '355 patent merely states that this ingredient "may be added to adjust the final formulation to isotonicity as well as a stabilizing aid during drying." (Col. 4, lines 12-14). There is no teaching or suggestion provided by the '355 patent to modify the basic method described in this patent so as to arrive at the presently claimed process,

which includes combinations of steps and amounts of ingredients, which function to allow the achievement of a rapidly dispersible solid dosage form of a drug. There is also no teaching or suggestion provided in the '355 patent that allows one skilled in the art to know to combine bulking/releasing agents with an aqueous suspension of drug and surfactant/phospholipid in the amounts specified so that the steps and elements therein function to produce a solid dosage form of the drug having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the Applicants. Furthermore, the '355 patent does not contemplate or teach a rapidly dispersible form of a drug. Accordingly, the '355 patent does not make obvious the presently amended claims. Withdrawal of this rejection is thus respectfully requested.

U.S. Patent No. 6,228,399

Claims 50-124 were rejected under the judicidally created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-5 of U.S. Patent No. 6,228,399 ("the '399 patent"). The Examiner states that the conflicting claims are not identical, but are allegedly not patentably distinct from each other because the claims in the '399 patent, which are drawn to "a process of preparing microparticles of water insoluble drug, cyclosporine by mixing the drug, a phospholipid and another surfactant and applying energy to reduce particle sizes", recite comprising language and that "applicant's intent to include bulking material such as mannitol in the comprising language is clear from the examples" in the cited patent. The Examiner opines that the "instant steps of adding the bulking materials" are deemed to be included in the patented method claims and that "water insoluble drug includes cyclosporine" in the '399 patent claims.

Applicants disagree with this rejection and submit that although the claims of the '399 patent contain comprising language, there is no teaching or disclosure in the '399 patent that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success. The mere disclosure of mannitol in the Examples of the specification of the '399 patent does not make obvious Applicants' inventive process, considered in its entirety, including the steps and elements therein, which specify and describe particular amounts and functions of bulking/releasing agents. The combination of steps and elements therein, including bulking/releasing agents, contributes to the newly described

properties of high dispersibility imparted to a solid dosage form that is produced by Applicants' presently claimed process. The steps and elements therein that constitute the process of the presently claimed invention are not found in the disclosure of the '399 patent.

The disclosure relating to mannitol in the '399 patent merely states that this ingredient "may be added to adjust the final formulation to isotonicity as well as a stabilizing aid during drying." (Col. 4, lines 31-34). There is no teaching or suggestion provided by the '399 patent to lead one having skill in the art to modify the basic method described in this patent so as to arrive at the presently claimed process, which includes combinations of ingredients in specified amounts and having specified functions allowing the achievement of a rapidly dispersible solid dosage form of a drug. There is also no teaching or suggestion provided in the '399 patent that allows one skilled in the art to know to combine bulking/releasing agents with an aqueous suspension of drug and surfactant/phospholipid in the amounts specified so that the steps and elements therein function to produce a solid dosage form of the drug having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the Applicants. Furthermore, the '399 patent does not contemplate or teach a rapidly dispersible form of a drug. Accordingly, the '399 patent does not make obvious the presently amended claims. Withdrawal of this rejection is thus respectfully requested.

U.S. Patent No. 6,465,016

Claims 50-124 were rejected under the judicidally created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent No. 6,465,016 ("the '016 patent"). The Examiner states that the conflicting claims are not identical, but are allegedly not patentably distinct from each other because the claims in the '016 patent, which are drawn to "a process of preparing microparticles of water insoluble drug, cyclosporine by mixing the drug, a phospholipid and another surfactant and applying energy to reduce particle sizes", recite comprising language and that "applicant's intent to include bulking material such as mannitol in the comprising language is clear from the examples" in the cited patent. The Examiner opines that the "instant steps of adding the bulking materials" are deemed to be included in the patented method claims and that "water insoluble drug includes cyclosporine" in the '016 patent claims.

Applicants disagree with this rejection and submit that although the claims of the '016 patent contain comprising language, there is no teaching or disclosure in the '016 patent that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success. The mere disclosure of mannitol in the Examples of the specification of the '016 patent does not make obvious Applicants' inventive process, considered in its entirety, including the steps and elements therein, which specify and describe particular amounts and functions of bulking/releasing agents. The combination of Applicants' process steps and elements therein, including bulking/releasing agents, contributes to the newly described properties of high dispersibility imparted to a solid dosage form that is produced in accordance with Applicants' presently claimed process. The steps and elements therein that constitute the process of the presently claimed invention are not found in the disclosure and claims of the '016 patent, which are directed to a process of stabilizing solid cyclic oligopeptide cyclosporine microparticles and compositions comprising the microparticles prepared by this process.

The disclosure relating to mannitol in the '016 patent merely states that this ingredient "may be added to adjust the final formulation to isotonicity as well as a stabilizing aid during drying." (Col. 13, lines 23-25). There is also no teaching or suggestion provided in the '016 patent that allows one skilled in the art to know to combine bulking/releasing agents with an aqueous suspension of drug and surfactant/phospholipid in the amounts specified so that the steps and elements therein function to produce a solid dosage form of the drug having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the Applicants. Furthermore, the ''016 patent does not contemplate or teach a rapidly dispersible form of a drug. Accordingly, the '016 patent does not make obvious the presently amended claims. Withdrawal of this rejection is thus respectfully requested.

Co-pending patent application U.S. Serial No. 10/443,772

Claims 50-124 were provisionally rejected under the judicidally created doctrine of obviousness-type double patenting over claims 1-44 of co-pending application U.S. Serial No. 10/443,772 ("the '772 application"). The Examiner states that the subject matter claimed in the instant application is fully disclosed in the co-pending '772 application, which is claiming

common subject matter. According to the Examiner, the claims directed to "water insoluble drug" are deemed to include fenofibrate in the claims of the co-pending '772 application.

Applicants submit herewith a terminal disclaimer, accompanying documentation and fee. Accordingly, withdrawal of this rejection is respectfully requested.

Co-pending patent application U.S. Serial No. 10/260,788

Claims 50-124 were provisionally rejected under the judicidally created doctrine of obviousness-type double patenting over claims 1, 2, 4-25, 45-47, 52, 53, 55, 56, 65 and 101-119 of co-pending application U.S. Serial No. 10/260,788 ("the '788 application"). The Examiner states that the conflicting claims are not identical, but they are allegedly not patentably distinct from each other because "the claims in the co-pending application are drawn to the same process of preparation and the products resulting from said process and the process is directed to water insoluble drugs." The Examiner further opines that the comprising language of the claims of the '788 application provides for the inclusion of a step of adding bulking materials such as mannitol, as claim 115 in the '788 application recites mannitol.

Applicants disagree with this provisional rejection and submit that although the claims of the '788 application contain comprising language, there is no teaching or disclosure in the '788 application that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success. The mere disclosure of mannitol in the Examples of the specification of the '788 application, and the recitation of mannitol as a stabilizing agent in the dependent claims of the '788 application, does not make obvious Applicants' inventive process, considered in its entirety, including the steps and elements therein, which specify and describe particular amounts and functions of bulking/releasing agents. The combination of Applicants' process steps and elements therein, including bulking/releasing agents, contributes to the newly described properties of high dispersibility imparted to a solid dosage form that is produced in accordance with Applicants' presently claimed process.

The steps and elements therein that constitute the process of the presently claimed invention are not found in the disclosure and claims of the '788 application, which are directed

to a process for preparing solid microparticles of a water-insoluble of poorly water soluble compound in an aqueous medium. The '788 application contains no recognition of Applicants' presently claimed process of producing a highly dispersible solid dosage form of a drug in which the process, considered in its entirety, involves steps and elements thereof that function together to achieve the claimed parameters and to produce the rapidly dispersible solid product.

The disclosure relating to mannitol in the '788 application merely states that this ingredient "may be added to adjust the final formulation to isotonicity as well as acting as a stabilizing aid during drying." (page 9, [0030] of the '788 application). There is no teaching or suggestion provided by the '788 application to lead one having skill in the art to modify the basic method described in this application so as to arrive at the presently claimed process, which includes combinations of ingredients in specified amounts and having specified functions allowing the achievement of a rapidly dispersible solid dosage form of a drug. There is also no teaching or suggestion provided in the '788 application that allows one skilled in the art to know to combine bulking/releasing agents with an aqueous suspension of drug and surfactant/phospholipid in the amounts specified so that the steps and elements therein function to produce a solid dosage form of the drug having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the Applicants. Furthermore, the '788 application does not contemplate or teach a rapidly dispersible form of a drug. Accordingly, the '788 application does not make obvious the presently amended claims. Withdrawal of this rejection is thus respectfully requested.

CONCLUSION

Applicants respectfully submit that the present application is now in condition for allowance. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this Amendment, or during the pendancy of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**; Reference No. **28069-546**; Customer No. **35437**.

Should any further extension of time be required for the timely consideration of this Amendment and response, the Commissioner is hereby authorized to grant any such further extension of time as may be necessary, and to charge any additional fee(s) owed by Applicants for such extension of time, to the above-mentioned Deposit Account, Reference and Customer Numbers.

If the Examiner believes that further discussion of the application would be helpful, he is respectfully requested to telephone Applicants' undersigned representative at (212) 692-6742 and is assured of full cooperation in an effort to advance the prosecution of the instant application and claims to allowance.

Respectfully submitted,

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.

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By: Leslie A. Serunian
Leslie A. Serunian
Registration No. 35,353

Correspondence/Mailing Address:
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
Chrysler Center
666 Third Avenue
New York, New York 10017
Telephone: (212) 935-3000
Facsimile: (212) 983-3115
Direct Tel.: (212) 692-6742

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